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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,099	04/12/2001	R. Shoshana Bamdad	M01015/70034 TJO	2967

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	13

DATE MAILED: 01/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/835,099	Applicant(s) BAMDAD ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,15,16 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-4, 15-16 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Summary of Action

I. The objection of claim 2 will not be maintained in light of the amendment.

II. The rejection of claims 1-2 and 3-10 under 35 USC 112, second paragraph, will not be maintained in light of the amendment.

III. Claims 3-4, 15-16 and 20-22 are rejected under 35 USC 112, 1st paragraph.

IV. Claims 4 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Asthana et al. (Clinical Pharmacology and Therapeutics, 1995, 58(3), 299-309).

V. Claims 3 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asthana et al. (Clinical Pharmacology and Therapeutics, 1995, 58(3), 299-309) in view of Giacobini et al. (Annals of the New York Academy of Sciences, 1996, Jan. 17, 777, 393-8).

Status of Application

1. By Amendment filed September 22, 2003, Claims 1, 2, 5-14, 17-19 and 23-123 have been cancelled and Claims 3, 4, 15, 16 and 20-22 have been amended.

2. Claims 20 and 21 were withdrawn from the examination as the non-elected invention based on applicants' election of Group I(f) and physostigmine as the elected species (Paper No. 8). Accordingly, claims 20 and 21 will not be examined as the elected invention in this Office action.

3. The applicants' amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3-4, 15-16 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduction or treatment of beta-amyloid aggregate formation in a patient susceptible to or exhibiting the specific symptoms of Alzheimer's Disease, does not reasonably provide enablement for "promoting the inhibition of beta-amyloid aggregate formation". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: nature of the invention, breadth of the claims, state of the art, relative skill of those in the art, predictability of the art, guidance of the specification, the working examples and the quantity of experimentation necessary. All the factors have been considered with regard to the claim, with the most relevant factors discussed below.

Although the amend claims have been presented with languages "promoting the inhibition", the scope of the claims still read on the prophylactic use of the claimed composition since the claims require the administration of the claimed composition prior to onset of the diseases or symptoms of the diseases.

Nature of the Invention: All rejected claims are drawn to the methods of promoting inhibition or treatment of beta-amyloid aggregate formation in patients susceptible to or exhibiting symptoms of Alzheimer's diseases with the administration of the instant composition.

Breadth of Claims: The breadth of the claims encompasses not only the treatment of beta-amyloid aggregate formation, but also inhibition (complete) or elimination (total) or prevention of the condition.

State of the Art: The state of the art does not recognize the administration of compositions to inhibit (completely), eliminate (totally) or prevent the condition as required in the instant claims. The state of the art recognizes the reduction or decrease or treatment of beta-amyloid aggregate formation, but not their complete inhibition or cure or prevention.

Relative Skill of Those in the Art: The relative skill of those in the pharmaceutical art is high.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to completely preventing the condition in mammals with the administration of the instant composition makes practicing the claimed invention unpredictable in terms of the prevention of the condition.

Guidance of the Specification: The guidance given by the specification on how to completely inhibit or prevent the claimed condition is absent. Guidance for reduction of beta-amyloid aggregate formation (page 47, line 19 thru page 52, line 29) is provided, however, no evidence that the condition is prevented or completely inhibited is provided.

Presence or Absence of Working Examples: As stated above, the specification provides inadequate working examples for the claimed invention.

The Amount of Experimentation Necessary: As stated above, the art demonstrates reduction or treatment of beta-amyloid aggregate formation, but does not provide enablement for the claimed prophylactic use. Therefore, the practitioner would turn to trial and error experimentation to use the instant composition for preventing the claimed condition, without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

For examination purposes, the phrase "promoting the inhibition" is interpreted as the "reduction" or "treatment" of the instant condition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 4 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Asthana et al. (Clinical Pharmacology and Therapeutics, 1995, 58(3), 299-309).

The claims are drawn to a method of treating patient susceptible to or exhibiting symptoms of Alzheimer's disease by reducing beta-amyloid aggregate formation, comprising administering physostigmine to the patient.

Asthana teaches the use of physostigmine as a cholinesterase inhibitor for treating patients with Alzheimer's disease by improving the cognitive dysfunction.

Although the reference is silent about the underlying pharmacological mechanism of physostigmine in "promoting the inhibition or treatment of beta-amyloid aggregate formation", such feature or property is deemed to be inherent to the referenced teaching of administering physostigmine to patients having Alzheimer's disease. As stated above, both the reference and the instant invention are directed the administration of same composition inherently possessing a therapeutic effect for the same ultimate purpose as disclosed by applicants. Therefore, the reference anticipates the claimed invention even absent explicit recitations of the mechanism of action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 3 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asthana et al. (Clinical Pharmacology and Therapeutics, 1995, 58(3), 299-309) in view of Giacobini et al. (Annals of the New York Academy of Sciences, 1996, Jan. 17, 777, 393-8).

As stated above in 35 USC 102(b) rejection, Asthana teaches the use of physostigmine in treating Alzheimer's disease patient, particularly symptoms of cognitive impairment.

Giacobini teaches or suggests the use of physostigmine in activating APP processing and decreasing the formation of amyloidogenic APP products such as beta-amyloid in Alzheimer's disease patient (abstract; page 393, para 1 thru page 394, para 1; conclusion).

The teaching of Asthana differs from the claimed invention in the use of physostigmine in "the patient is susceptible to but does not exhibit symptoms of Alzheimer's disease" required in claim 3; "the patient is free of indication for treatment for central nervous system neuronal damage, as caused by aggregate formation" required in claim 15 and "wherein the patient is free of symptoms of dementia" required in claim 16. To incorporate such teaching into the teaching of Asthana, would have been obvious in view of Giacobini who teaches the underlying

pharmacological mechanism of physostigmine in activating APP processing and decreasing the formation of beta-amyloid in Alzheimer's disease patient.

Above references in combination make clear that activating APP processing with physostigmine would decrease or retard the deposition of amyloid, thereby serving as an effective treatment for a disease in an individual in which amyloid is deposited in the brain, for example Alzheimer's disease. One having ordinary skill in the art would have recognized that the underlying mechanism to explain a slower deterioration of Alzheimer's disease is mediated thru the activity of physostigmine in activating APP processing and decreasing beta-amyloid deposition. Furthermore, one having ordinary skill in the art would have expected that physostigmine would be useful in treating various symptoms resulted from the amyloid deposition (depending upon the location of the amyloid is deposited). Therefore, one having ordinary skill in the art would have been motivated to administer physostigmine that suppresses or retards the deposition of amyloid, with the reasonable expectation of success, to treat other symptoms of Alzheimer's disease or Alzheimer's patient free of symptoms of central nervous system neuronal damage, as caused by the amyloid deposition, specifically free of symptoms of dementia. One having ordinary skill in the art would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about.

With respect to claim 3, the claim relates the administration of physostigmine to the patient before the appearance of symptoms of the Alzheimer's disease in order to slow the onset of the symptoms. As stated above, the prior art references disclose the administration of

physostigmine to the patient after the patient has begun to show symptoms of Alzheimer's disease to alleviate or slow the further progression of the disease, but they are silent about the administration of physostigmine to the patient before the appearance of symptoms of the Alzheimer's disease, namely "the patient is susceptible to but does not exhibit symptoms of Alzheimer's disease". Generally, differences in time differences (before or after the appearance of symptoms of Alzheimer's disease) will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such time periods are critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable time periods by routine experimentation.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600